July, 2001

Responses to Comments Submitted by Western States Petroleum Association on Diesel Exhaust Particulate

Overall Comment: The Western States Petroleum Association (WSPA), wish to submit these comments on the listing of diesel exhaust particulate (DEP) in the "Tier 1" category and on the background document that OEHHA has prepared on this substance. As you know, WSPA has been actively following this issue for some time and this issue continues to be a high priority for our members.

We note that OEHHA's previous draft placed DEP in the "Tier 2" group because the data for adverse effects on children were primarily indirect and not as strong as for other compounds under consideration. Our reading of the available material indicates that this is still the case with respect to causality, exposure and susceptibility. Therefore, we see no basis to place the material in Tier 1. The rationale presented by OEHHA is based on five lines of evidence; 1) Enhancement of allergic responses; 2) Traffic density studies; 3) General ambient PM10 health effects; 4) PAHs found in DEP; and 5) Developmental and reproductive effects. We provide some very brief comments these issues below.

Comment 1: Enhancement of Allergic Responses

The findings of biochemical changes in response to exposure to DEP are of interest and the potential for an adjuvant response should be investigated more thoroughly (Mauderly, 2001). However it must be emphasized that biochemical indicators are not the same as an observed increase in symptoms, and intratracheal (or intranasal) instillation of high levels of DEP is not the same as inhalation exposure of low levels of DEP. Thus while the findings to date may lead one to hypothesize about effects on asthma and allergy severity, there remains a lack of direct evidence in this area. It remains to be determined whether the adjuvant effect is significant at current environmental exposure levels, and whether the effect is unique to DEP. The level of evidence at this point in time does not justify the placement of DEP in Tier1. This is especially true when one compares the strength of evidence for diesel with other toxic air contaminants (e.g. formaldehyde) that have been reviewed in this process and that were not included in the Tier 1 list.

Response 1: Diesel exhaust particulate matter causes adverse immune system effects that may result in adverse health outcomes (e.g. possible exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., , 2000; and many others, see summary of diesel exhaust particulate pp. 7-13); these adverse immunological effects are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden *et al*., 2000). Additionally, acute exposures of healthy adult humans to concentrations of diesel exhaust particulate matter (300 $\mu g/m^3$) approximately one order of magnitude greater than peak diesel exhaust concentrations noted near California freeways demonstrated a marked leukocytic airway infiltration accompanied by enhanced chemokine and cytokine production (Salvi *et al.*, 2000). It should be noted that 300 $\mu g/m^3$ was a LOEL (Lowest Observable Effect Level) in this study. Lower concentrations of

diesel exhaust particulate matter were not tested, raising the possibility that these effects may be observed at concentrations lower than 300 $\mu g/m^3$. Additionally, Frew *et al.* (2001) observed upregulation of IL-10 production in the bronchial epithelium of asthmatic subjects but not healthy subjects at a PM_{10} concentration of only 108 $\mu g/m^3$. The authors stated that the observed IL-10 upregulation may alter the airway biology towards a more allergic phenotype. It is also possible that healthy and/or asthmatic children may be more sensitive to diesel exhaust particulate matter-induced immune system effects than healthy adults. These data indicate that diesel exhaust particulate matter adversely impacts healthy adult immune systems at concentrations close to those observed in cars driving on California freeways (e.g., up to 23 $\mu g/m^3$), making them very relevant to a consideration of diesel exhaust particulate matter for prioritization under SB 25.

Comment 2: Traffic Density Studies

Several studies are cited that indicate an increase in respiratory symptoms associated with proximity to roadways. It should be pointed out that DEP is only one component of the particulates that are generated by roadway traffic, and in most of the studies cited, it was not even measured. Such studies are also subject to multiple potentially confounding factors. In our previous comments we noted several studies that did not show these traffic related effects. These studies continue to be ignored in this draft. It does not seem useful to either the SRP or the public to present only results that indicate positive effects while leaving out others that show a different outcome. Thus, as a whole, the traffic density line of evidence is also very weak with regard to showing a differential health risk to children. While the data is still forthcoming, some information from the recent OEHHA symposium at UCLA seemed to show that particulate matter from vehicle use (i.e., brake dust, tire wear, re-entrained road dust from other sources) rather than simply DEP could be significantly contributing to asthma in children.

Response 2: This document discusses the uncertainties associated with the adverse health effects reported for the TACs, and includes descriptions of negative studies where appropriate. We considered the studies and comments previously submitted. However, it is not necessary to include a detailed description of every negative study for the prioritized TACs in the literature. Since the purpose of the current review was to identify any potential for differential effects on infants and children, OEHHA concentrated on those studies which contained information on this issue, and did not include in the toxicity summary a number of studies which are uninformative on this point.

The comment points out the difficulty of evaluating epidemiological studies to pinpoint causative agents. However, the statute requires OEHHA to consider multiple pollutant exposures. Therefore, if there is an association between PM_{10} and other co-pollutant and an adverse health effect, that information must still be considered. Most of the studies that looked at respiratory health impacts of traffic-related pollutants specifically looked at truck traffic, which in the countries where the studies were done is all diesel-fueled. Truck traffic density was the metric associated with adverse respiratory health impacts. In addition, one of the studies measured

PM_{10} and soot (largely $PM_{2.5}$) as well as truck traffic density. The strongest correlation with adverse respiratory health impacts in this study (Brunekreef et al, 1996) was with soot, which in these environments is largely from diesel-fueled engines.

It is generally agreed that asthma causation is multifactorial. OEHHA does not state that increased asthma rates in children are due to exposure to diesel exhaust particulate. Rather the evidence from immune toxicity studies of diesel exhaust particulate indicates enhancement of allergic responses even to neoallergens. This, in conjunction with epidemiology studies of asthma exacerbation by particulate air pollution and studies of respiratory health in children living near busy roadways, is reason to believe that diesel exhaust particulate exacerbates asthma and possibly contributes to new asthma cases. OEHHA has also noted in the prioritization document and in its response to comments that no direct epidemiological evidence of differential sensitivity of children to asthma induced specifically by diesel exhaust particulate matter (as opposed to PM_{10} or $PM_{2.5}$) has been published. OEHHA considers asthma to impact children more than adults because of the higher prevalence rates and hospitalizations rates for asthma in children compared to adults. The possibility that diesel exhaust particulate matter may differentially impact children stems from the mechanistic data indicating that diesel exhaust particulate matter exerts specific adverse immune system effects potentially related to asthma and other immune system-related diseases.

Comment 3: General Ambient PM10 Health Effects

As noted in previous comments, many associations have been observed between ambient particulate matter and health effects, but there is little evidence to conclude that DEP is more or less likely to be a causative agent as compared to other components. This is still an active area of research. The information presented by OEHHA would actually lead one to the opposite conclusion. Since the proportion of ambient PM that is composed of DEP varies substantially between cities, and if the effects of PM10 are quantitatively similar across these different cities, this suggests that DEP is not the primary culprit. This does not make a good argument for a differential effect of DEP (as a Toxic Air Contaminant) on children. Particulates as a group are already being reviewed under a separate provision of SB25.

With regard to infant mortality, in our previous comments (both oral and written) we pointed out the article by Lipfert et al. (2000) that discussed geographic confounding in the attribution of PM10 to infant mortality. This very relevant work should be cited in the report (if OEHHA decides to retain the PM10 section of the chapter).

Response 3: There are now a dozen or more studies which evaluated exacerbation of symptoms in asthmatics and air pollution, and hundreds of studies on cardiopulmonary morbidity and mortality associated with exposure to PM_{10}. Many of these studies find a positive association of adverse respiratory and cardiovascular effects with PM_{10}. These studies were done in Europe, the U.S., Mexico, South America, and British Columbia in areas with very different mixes of pollutants. The comment notes that the PM associated adverse health effects have been noted in

a number of cities with differing particulate matter composition, and uses this as a reason to discount the contribution of diesel exhaust particulate to these effects. OEHHA looks at this in quite an opposite light. Since some of the studies which observed an association between PM and asthma, cardiopulmonary morbidity and mortality, and infant mortality were done in cities where the vast majority of particulate was from diesel-fueled engines, then it is extremely difficult to discount a contribution from diesel exhaust particulate to the observed effects. There certainly was not a protective effect in those cities with a large diesel exhaust particulate contribution to PM.

Comment 4: Diesel Particulates Contain PAHs

There is no doubt that diesel particulates contain PAHs, however what is relevant from a toxicological standpoint is the level of dose that would be delivered to target organs. Extractions of high levels of PAH for direct application are of little relevance in answering questions of differential susceptibility to the effects of DEP.

Response 4: The bioavailability of PAHs contained in diesel exhaust was thoroughly reviewed in the diesel exhaust TAC document (OEHHA, 1998). The studies reviewed included occupational exposure studies, and clearly indicated that the PAHs in diesel exhaust were bioavailable upon inhalation exposure. Additionally, a recent study by Sato *et al.* (2000) indicated that rats exposed to diesel exhaust by inhalation demonstrated increased mutations in a reporter gene and covalent DNA adducts, additional evidence suggesting PAH bioavailability. These studies, especially those involving occupational exposures, suggest that the PAH levels present in ambient diesel exhaust particulate matter are toxicologically relevant.

Comment 5: Developmental and Reproductive Effects

The interpretation of the study by Watanabe and Kurita (2001) is incorrect. These authors found the same difference in anogenital distance whether they exposed animals to diesel exhaust or diesel exhaust that had been filtered to remove DEP. The authors concluded that the gaseous phase must have included the relevant toxicants. Furthermore, the exhaust stream contained other compounds associated with combustion as well as products of incomplete combustion. Until one looks at other exhaust streams, (i.e., gasoline, methanol, CNG), it is unclear that the results are due to diesel exhaust and not other components such as NOx.

Furthermore, there is no basis to state on the top of page 26 that it is "plausible" that DEP is a teratogen because PAHs show this effect. There is absolutely no consideration of dose/ response relationships in such a statement. It is also just as plausible that grilled hamburgers and a multitude of other foods are teratogenic using this same logic (since they contain PAHs). Is orange juice a plausible teratogen because it contains ethanol? These statements implying teratogenicity of DEP should be removed from the report.

Response 5: The comment correctly points out that exposure to both unfiltered and filtered diesel exhaust resulted in masculinization of the fetus in Watanabe and Kurita (2001). However, some of the chemicals that might plausibly be associated with this effect (e.g., dioxins, PAHs) exist in the particulate and gaseous phases of the exhaust depending on temperature, dilution processes, and so forth. Until the toxicants responsible for this endocrine effect are identified, it is premature to ascribe the effect solely to the gaseous phase of diesel exhaust.

Diesel exhaust PAHs have been demonstrated to be bioavailable at occupational exposure levels, and PAHs have been demonstrated to have teratogenic effects. The data indicate that it is therefore plausible (i.e., worthy of consideration as a hypothesis) that such effects would also result from exposure to diesel exhaust due to its PAH content. Further, the prioritization document does not state that the available data are sufficient for a determination that diesel exhaust is a teratogen, and acknowledges that "it does not appear that the endpoints observed for PAH developmental toxicity have been adequately evaluated for diesel exhaust exposure".